International Supply Chain for Unapproved Medicines

Dr. Keith Watts
Executive Vice President, Strategic Services, One-World, Inc.
Managed Access Program Implementation areas through Expanded Access Protocols:

- Enhance and streamline the delivery of specialty pharmaceuticals that address unmet medical needs around the world
- Match patients across the globe with serious diseases to needed therapies prior to registration or product approval
- Understand the requirements that are associated with charging for treatment
- Establish a cost share model for an expanded access program and protect global pricing for future sales
- Garner insight on the reporting and reimbursement process on an international scale
Meeting Unmet Medical Needs

Product Lifecycle Support

Neglected ethical access to desperately needed medicines
3.1 Market Definition

**Single Patient, On-Demand, Emergency Use,**

a) As part of an existing IND; use not primarily intended for safety/efficacy evaluation

b) Patient does not qualify for a clinical trial; standard treatment has failed & no Tx alternatives; have a Dx for which the drug has demonstrated activity; benefits outweigh the risks

c) Use of approved drug not yet licensed in local market (e.g. ex-US)

d) Use of approved drug where availability is limited by a REMS\(^1\) program

**Intermediate-size Population, Cohort or Group Authorizations**

a) As part of an existing IND; use not primarily intended for safety/efficacy evaluation.

b) Patients not qualifying for a clinical trial, critical unmet medical needs; benefits>risks

c) In France, known as a cohort ATU

**Large Patient Populations**

a) Population under Treatment IND or Treatment Protocol (i.e. from clinical trial)

b) Most commonly following clinical trial, but prior to product approval\(^2\)

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\(^1\) REMS: Risk evaluation and mitigation strategy. Could include Medication Guide distribution, communication plan including limited provider and patient education; Other as determined by regulatory body.

Metrics of Success

• Manage the supply chain, compliantly, securely, and rapidly
  • Patient Metrics
  • Provider Metrics
  • Manufacturer Metrics
Program Model

• Program Model:
  • NPP
  • Cohort – non-trial, medium population
  • Cohort – Trial Transition, large population
  • Clinical Trial Drug Supply

• Financial Model*
  • On-Demand: Purchase/Sale – reimbursement generally available for on-demand
  • Early & Expanded Access: Pre-registration access in conjunction with and following completion of a clinical trial. Fee-for-Service (Compassionate Use Programs) or Purchase/Sale with safety, AE reporting standard (where reimbursement mechanisms exist)
  • Compassionate Use: Fee-for-Service arrangement usually the preferred arrangement where allowed by local regulations, subject to client pricing model and commercialization objectives
Geographic Experience

• Major Markets
  • Europe (Western)
  • US

• Evolving Markets
  • Asia-Pacific
  • Latin America
  • Eastern Europe
  • Middle East/North Africa
### EAP Financing Sources by Region

<table>
<thead>
<tr>
<th>DRAFT</th>
<th>Government Pay</th>
<th>Private Pay</th>
<th>Manufacturer Pay (Compassionate Use)</th>
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</thead>
<tbody>
<tr>
<td><strong>Asia Pacific</strong></td>
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<td></td>
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<tr>
<td>Australia/NZ</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Japan/S. Korea</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>China</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Other</td>
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<td>X</td>
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<tr>
<td><strong>Eastern Europe</strong></td>
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<tr>
<td>Russia</td>
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<td>X</td>
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<tr>
<td>Other</td>
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<tr>
<td><strong>Middle East/No. Africa</strong></td>
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<tr>
<td>Saudi/UAE</td>
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<td>X</td>
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<tr>
<td>Iraq/Yemen</td>
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<td>X</td>
<td>X</td>
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<tr>
<td>North Africa</td>
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<td></td>
<td>X</td>
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</tbody>
</table>
### 3.1 Market Definition by Region

<table>
<thead>
<tr>
<th>Protocols</th>
<th>US</th>
<th>Europe (EU)</th>
<th>Europe (non-EU)</th>
<th>Asia Pacific</th>
<th>So. Am. (Brazil)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mature</strong></td>
<td>Mature</td>
<td>Complex</td>
<td>Complex</td>
<td>Complex</td>
<td>Complex</td>
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<tr>
<td><strong>Evolving</strong></td>
<td>X</td>
<td>X</td>
<td>Evolving</td>
<td>X</td>
<td>Evolving</td>
</tr>
<tr>
<td><strong>Named Patient Basis</strong>¹ (Treatment IND)</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
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<tr>
<td>“Single Patient, Emergency Use”</td>
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<tr>
<td>Named Patient Basis or Program (NPP)</td>
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<tr>
<td><strong>Expanded Access</strong></td>
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<tr>
<td>“Intermediate Population”</td>
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<tr>
<td>Expanded Access</td>
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<tr>
<td><strong>Cohort Program (Need)</strong> (EU: Early Access)</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>X</td>
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<tr>
<td>(Compassionate Use²)</td>
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<tr>
<td>“Large Population”</td>
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<td>Early Access</td>
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1. **Named Patient Basis**¹ (Ex-US) – regulatory pathway for pre-approval access to a product at MD request for patient with unmet medical need.

2. **Compassionate Use**— also referred to broadly as Expanded Access in ROW countries; regulatory pathway ex-US to a pre-determined group of patients outside scope of clinical trial, in cooperation with MD, Institution, or government depending on local regulation.
3.1 EAP Governance

<table>
<thead>
<tr>
<th>Region</th>
<th>Stage</th>
<th>Governing Body and Legislation</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>Mature</td>
<td>FDA: CFR 21 Sec 312.300-320</td>
</tr>
<tr>
<td>Europe (EU)</td>
<td>Mature</td>
<td>European Medicines Agency (EMA); Implementation governed by individual country legislation. Patient W.A.I.T. 116-241 days; Launch lag in EU from 2-12 mo.¹</td>
</tr>
<tr>
<td>Europe (non-EU)</td>
<td>Complex; Evolving</td>
<td>Complex to navigate; Evolving markets re: regulatory pathway</td>
</tr>
<tr>
<td>Asia Pacific</td>
<td>Mature</td>
<td>Australia; NZ; Japan; Singapore; Korea; South Africa</td>
</tr>
<tr>
<td>South America</td>
<td>Evolving</td>
<td>Brazil most evolved. See below.</td>
</tr>
<tr>
<td>Brazil</td>
<td>Complex; Evolving</td>
<td>ANVISA; Each patient, requires approvals and coordination between 3 Federal Agencies, the state (7), and local municipality (29) where physician/patient resides</td>
</tr>
<tr>
<td>Central America</td>
<td>Evolving</td>
<td></td>
</tr>
</tbody>
</table>

Major Markets

• Europe (West; East latest market expansion)
• Middle East
• China (Hong Kong)
• South Pacific (Australia, NZ, Japan)
• South Africa & West Africa
• South America & Central America
  • Brazil
  • Chile
  • Columbia
  • Argentina
  • Paraguay, Uruguay, Bolivia, Panama
Europe EAP
NPP – Cohort – Large Cohort

- Oslo
- Stockholm
- Copenhagen
- London
- Ibbenbüren
- Lodz
- Bartenheim
- Zurich
- Zagreb
- Budapest
- Lisbon
Population: approx. 200 mio.
26 states + Brasilia
27 governments
25% of population located in:

• Recife
• Brasilia
• Belo Horizonte
• Rio de Janeiro
• Sao Paolo
• Porto Allegre

Brazil EAP
NPP – Cohort – Large Cohort
Needed Capabilities

- Operational Plan and EAP Advising
- Regulatory & Customs Application (EAP)
- Assumption of Reimbursement Financial Risk
- Sponsor Protocol or Med Affairs Coordination
- Drug Delivery to Provider (Institute or MD)
- Confirmation of Drug Delivery
- AE Reporting to Sponsor
Extended Capabilities to Support Global Access

- Market Insights
- Physician Education
- HQ Surrogate (Select Markets)
- Registration Filing (Select markets)
Case Study
Evolving Markets, Named Patient Access

Regional Implementation:
- Europe (EU) – Low Barriers
- Other Complex Countries – labor intensive, require in-market experts, patience and persistence
  - Europe – Non-EU, Italy
  - South America – labor intensive, different bus model re: customer relationships
  - Scandinavia – labor intensive, different bus model re: customer relationships
  - Hungary
  - China
  - Asia Pacific, (Australia, New Zealand, South Africa)

Example Brazil:
- Years experience with Brazil national and local state government entities to effectively, efficiently, and compliantly distribute specialty therapies on a managed access basis
- Long-standing relationships with required in-market Government Brokers and Distributors to navigate tender offers & distribution
- Extensive expertise with the multiple government entities required to get product to institution or patient
  - Ministry of Health
  - Health and Human Services (HHS of Brazil)
  - Customs (Brazil)
  - Local State Government entities (26 states) + Federal (Brasilia)
- Network of local validated shippers to efficiently and effectively deliver to institution or Physician
6. Conclusion
Appendix – Backup Slides
3.2 EAP Industry Overview

Market Size
• $3bn to $5bn in total sales potential
• Temozolomide – Germany, Switzerland, France, Brazil: $3.4MM w/average of 12 month EAP
• Harvoni – at negotiated rate (France) 1 cycle across all 4 countries: $1.63bn

Insights:
Even though there has been significant growth, EAP’s are still very niche oriented and evolving. The landscape is dynamic and continues to change requiring local resources providing competitive intelligence.

Trends:
• More countries are adapting some form of EAP’s due to pressure from the physician and patient communities
• Manufacturers are recognizing the value of developing the programs
• The unmet medical needs of many patients are being satisfied much earlier than with traditional MA

Drivers:
• Access to information from internet and socials media
• Hyper social awareness and sensitivities to the plights of others worldwide
• Perceptions that Big Pharma is more about profits than patient care perpetuated by the press

Risks:
• Clinical risk – adverse event due to improper protocols or education
• PR risk – negative publicity for not offering or meeting in-market demand